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10/802,197	03/17/2004	Claus D. Buergelt	5853-371	3776

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EXAMINER	
OGUNBIYI, OLUWATOSIN A	
ART UNIT	**PAPER NUMBER**
1645	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/802,197	BUERGELT ET AL.	
	Examiner	Art Unit	
	Oluwatosin Ogunbiyi	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *15-20* is/are withdrawn from consideration.

5)☒ Claim(s) *1-5* is/are allowed.

6)☒ Claim(s) *6-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO AMENDMENT

The amendment filed 5/1/2007 has been entered into the record. Claims 1-20 were pending in the application. Claims 15-20 were withdrawn as being drawn to non-elected invention. Claims 1-14 were examined and are currently under examination.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Objections to claim 1,2,6,10 and 14 are withdrawn in view of the amendments to the claims.

Rejections Withdrawn

1. The rejection of claims 1-14 under 35 USC 1st paragraph scope of enablement is withdrawn in view of the amendments to the claims to include a nucleic acid extraction step.
2. The rejection of claims 1-5 under 35 USC 112, 2nd paragraph as being incomplete for omitting essential steps of detecting a PCR product of a particular size is withdrawn in view of Applicants amendment to the claims to recite primers SEQ ID NO: 1 and SEQ ID NO: 2.

3. The rejection of claims 1,3 and 14 under 35 USC 102(b) as being anticipated by Englund et al, Diagn Microbiol Infect Dis 33:163-171,1999 is withdrawn in view of the amendment to claim 1 which now recites SEQ ID NO: 1 and SEQ ID NO: 2 and the amendment to claim 14 which now recites 413 base pairs.

4. The rejection of claims 1,3 and 14 under 35 USC 102(b) as being anticipated by Erume et al. African Health Science, 2001, 1:83-89 is withdrawn in view of the amendment to claim 1 which now recites SEQ ID NO: 1 and SEQ ID NO: 2 and the amendment to claim 14 which now recites 413 base pairs.

5. The rejection of claims 1,3,4,5 and 14 under 35 USC 102(a) as being anticipated by Herrewegh et al. EP 1223225 A1 published July 17, 2002 is withdrawn in view of the amendment to claim 1 which now recites SEQ ID NO: 1 and SEQ ID NO: 2 and the amendment to claim 14 which now recites 413 base pairs.

6. The rejection of claims 1,2,3,5 and 14 under 35 USC 102(a) as being anticipated by Corti et al BMC Microbiology, 2002, 2:15 is withdrawn in view of the amendment to claim 1 which now recites SEQ ID NO: 1 and SEQ ID NO: 2 and the amendment to claim 14 which now recites 413 base pairs.

Rejections Maintained

7. The rejection of claims 6-14 under 35 USC 112, 2nd paragraph as being incomplete for omitting essential steps of detecting a PCR product of a particular size is maintained for reasons made of record in the office action mailed 12/22/2006.

Applicants argue that "it is clear that Applicants teach detection of Map using primers SEQ ID NOS: 1 and 2 which are nested primers. As is known by one of ordinary skill in the art, a nested primer pair produces an amplification product of a specific size. The information "333 base pair product" is extraneous and not required. Thus one of ordinary skill in the art would know the "metes and bounds" of the instant claim".

Applicants' argument is not persuasive. The claims as written omit the essential physical step of detecting a PCR product of a particular size. As such the claims further lack antecedent basis for the recitation 'wherein the presence of an amplification product specific for Map in the PCR reaction mixture indicates that the animal is infected with Map'.

As to the recitation of primers J1 and J2 and P90 and P91 as being laboratory designations without structural limitations to said primers, Applicants state that the claims have been amended to provide structural limitations for J1 and J2 by referring to their sequences.

However, this change is not reflected in claims.

As to the designation of P90 and P91, applicants state that "these are referred to by the region and size of the sequence generated and point to p.7 lines 19-24 of the specification".

However, line 19 of the specification states that "primers P90 and P91 for IS900 specifically recognize a 413bp sequence of Map. See Vary et al. Journal of Clinical Microbiology 28:933-937, 1990". Vary et al does not disclose primers named P90 and P91 nor discloses primer sequences for P90 and P91 that amplify a region of the IS900 region of Map. Therefore, the metes and bounds of J1 and J2 and P90 and P91 are not clear as recited in the claims, as they are laboratory designations. Hence, the rejection is maintained for reasons set forth in the previous office action.

8. The rejection of claims 6,7,8,9 and 11 under 35 USC 102(b) as being clearly anticipated by Englund et al is maintained for reasons set forth in the previous office action mailed 12/22/2006.

The claims are drawn to a method for detecting a Map infection in an animal, the method comprising the steps of:

(A) providing a biological sample from the animal and extracting nucleic acids from the sample;_and

(B) subjecting the extracted nucleic acids to nested polymerase chain reaction using at least a first pair of primers for amplifying the IS900 region of the *Mycobacterium avium subsp, paratuberculosis* (Map) genome and a second pair of primers for amplifying a

portion of the amplified IS900 region,

wherein the presence of an amplification product specific for *Mycobacterium avium subsp, paratuberculosis* Map in the polymerase chain reaction mixture indicates that the animal is infected with *Mycobacterium avium* subsp, paratuberculosis Map.

Applicants argue that in Englund et al., the nucleotide sequence differs from the instant primers J1, J2. The primers in Englund et al., specifically probes for only 210 base pairs in nested PCR, which is different to the instant 333 base pairs. Furthermore, these are directed to strain Linda, which was isolated from a patient with Crohn's disease and may not reflect bovine field strain MAP seen in cattle. Furthermore, Applicants have amended the claims to indicate the structural information for the instant primers.

This is not found persuasive.

Englund et al teach all the limitations of the claims including extraction of nucleic acids (see materials and methods as set forth in the previous office action). No structural limitations are recited in the claims 7,8 and 9 for primer pairs J1 and J2 and P90 and P91 which are mere laboratory designations and do not distinguish said primer pairs from the prior art. Claim 6 does not limit to a particular size of an amplification product. Furthermore, the claims do not recite particular strains of Map.

9. The rejection of claims 6,7,8,9 and 11 under 35 USC 102(b) as being clearly anticipated by Erume et al is maintained for reasons set forth in the previous office action mailed 12/22/2006.

The claims are set forth supra.

Applicants argue that there is only a 210bp product amplified and the sequences and alignments differ resulting in detection of less copies of the Map genome. Applicants argue that the claims have been amended to indicate the structural information for the instant primers.

This is not found persuasive.

Erume et al teach all the limitations of the claims including extraction of nucleic acid (see materials and methods as set forth in the previous office action). Claim 6 does not teach a particular size of an amplification product and the claims do not refer to the numbers of copies of the Map genome. Furthermore, no structural limitations are recited in the claims 7,8 and 9 for primer pairs J1 and J2 and P90 and P91 which are mere laboratory designations and do not distinguish said primer pairs from the prior art.

10. The rejection of claims 6,7,8,9,11,12 and 13 under 35 USC 102(a) as being clearly anticipated by Herrewegh et al is maintained for reasons set forth in the previous office action mailed 12/22/2006.

The claims are set forth supra.

Applicants argue that Herrewegh et al. conduct only one animal study. The base pair product discussed in Herrewegh et al. is extremely low and rather points to a degradation product. As such the primers completely differ as they do not give rise to the same base pair product. Furthermore, Applicants have amended the claims to indicate the structural information for the instant primers.

This is not found persuasive.

Herrewegh et al teach all the limitations of the claims as set forth in the previous office action including extraction of nucleic acids (see p.4 paragraph 16 as cited in the previous office action). The argument that Herrewegh conducts only one animal study is not convincing as the claims does not teach such limitation. Claim 6 does not teach a particular size of an amplification product and the Office does not have means for determining whether the amplification product of Herrewegh et al is a degradation product as asserted by Applicants representation. Furthermore, no structural limitations are recited in the claims 7,8 and 9 for primer pairs J1 and J2 and P90 and P91 which are mere laboratory designations and do not distinguish said primer pairs from the prior art.

11. The rejection of claims 6,7,8,9,10,11 and 13 under 35 USC 102(a) as being clearly anticipated by Corti et al is maintained for reasons set forth in the previous office action mailed 12/22/2006.

The claims are set forth supra.

Applicants argue that the Corti et al. primers are different in sequence and alignment from the instant invention. The primers in Cortis et al only detect 298 base pairs products different from the 333 base pairs of the instant invention and as such, detect less copies of the MAP genome. Furthermore, Cortis et al did not determine difference of results when only using primers P90, P91 and then followed by the nested PCR reaction. In addition, the PCR reaction was performed in bulk milk and not on milk obtained from individual animals as in the instant invention. Applicants have amended the claims to indicate the structural information for the instant primers. As such, Cortis et al., fails to teach each and every claim limitation of the instant invention.

This is not found persuasive.

Corti et al teach all the limitations of the claims as set forth in the previous office action including extraction of nucleic acids (see materials and methods p.4-6 as cited in the previous office action). Claim 6 does not teach a particular size of an amplification product and there are no structural limitations recited in the claims 7,8 and 9 for primer pairs J1 and J2 and P90 and P91 which are mere laboratory designations and do not distinguish said primer pairs from the prior art. Corti et al did perform a nested PCR reaction using a using a first pair of primers, primers P90 and P91 for amplifying the IS900 Map specific insertion sequence and a second pair of primers for amplifying of the first amplification product produced with primers P90 and P91 (see materials and methods). Applicants argument that the milk in Corti et al came from bulk milk instead from individuals is not found persuasive because the methods of Corti et al still

accomplish the task of detecting Map infection in an animal as the bulk milk is also obtained from at least one animal that is infected with Map.

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 7,9 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for detecting a Map infection in an animal, the method comprising the steps of:

(A) providing a biological sample from the animal and extracting nucleic acids from the sample; and

(B) subjecting the extracted nucleic acids to nested polymerase chain reaction using at least a first pair of primers for amplifying the IS900 region of the *Mycobacterium avium subsp, paratuberculosis* (Map) genome and a second pair of primers for amplifying a

portion of the amplified IS900 region,

wherein the presence of an amplification product specific for *Mycobacterium avium subsp, paratuberculosis* Map in the polymerase chain reaction mixture indicates that the animal is infected with *Mycobacterium avium* subsp, paratuberculosis Map, wherein the first pair of primers are primers P90 and P9, wherein said primers consist of the primers P90 and P91, wherein said primers recognize a 413 bp sequence of the IS900 region of *Mycobacterium avium* subsp. *paratuberculosis*.

The primers P90 and P91 are laboratory designations, which do not provide any structural limitation and do not distinguish from the prior art. The specification does not provide guidance as to the sequence of the primers P90 and P91 and only describes P90 and P91 as their ability to amplify a 413 base pair product of the IS900 region of Map.

The recitation of P90 and P91 does not convey a common structure for all primers that can amplify a 413bp product from any part of the IS900 region. There are no sufficient identifying characteristics the set of primers that can amplify any 413 bp product of IS900.

The scope of the claims encompasses numerous structural species of primers that can amplify any 413 bp product of IS900 region which is 1.45 kilobases (Vary et al. Journal of Clinical Microbiology, 1990, P. 933-937) resulting in a highly variant genus composed of members with a significant number of structural differences. The disclosure fails to describe the common attributes or structural characteristics that identify members of said genus of primers that can amplify a 413 base pair product of

IS900 and because the genus is highly variant, the recitation of P90 and P91 alone without structural limitation is insufficient to describe the genus of said primers.

One of skill in the art would reasonably conclude that the specification and claims lacks written description for primers P90 and P91 and the variant genus of any pair of primers that can amplify a 413 bp product of the IS900 region and one of skill in the art would not recognize that applicants had possession of the genus of the claimed pair of primer(s).

13. Claims 7,9 and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are set forth supra.

The nature of invention is drawn to primers P90 and P91 used as a first pair of primers in a nested PCR reaction used to detect Map infection in an animal. Said primers are not described by any structural limitation but by the amplification product of said primers which is a 413 base pair product.

Thus, the breadth of the claims encompasses detection of Map (*Mycobacterium avium paratuberculosis*) infection by nested PCR (polymerase chain reaction) using any first pair of primers that amplify the IS900 region of the Map genome. The recitation of primers P90 and P91 in the claims does not impart any limitations to the identity of the

primers in terms of their nucleotide sequence and does not impart any limitations as to the particular 413 base pair product. The specification does not define P90 and P91 in by structure. Thus, the claims are drawn to any pair of primers that amplify a 413 bp product.

The specification on p.7 line 19-20 teaches that primers P90 and P91 for IS900 specifically recognize a 413bp sequence of Map. See Vary et al. Journal of Clinical Microbiology 28:933-937, 1990. However, Vary et al do not disclose primers P90 and P91 or a 413 base pair product.

Although, the specification provides example of primers designated P90 and P91 used to amplify a 413 bp product, the specification does not provide guidance as to the particular 413 base pairs of IS900 region being amplified. IS900 of Map is 1.45 kilobases and therefore there are numerous possibilities for different 413bp amplification products (Vary et al. Journal of Clinical Microbiology, 1990, P. 933-937).

Thus, without the disclosure of the particular sequence of the primer pairs being used to amplify the instantly claimed 413 bp product it would require undue experimentation of one of the skilled artisan to practice the invention as claimed.

Status of Claims

Claims 6-14 are rejected. Claims 1-5 are free of art and allowable.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Oluwatosin Ogunbiyi whose telephone number is 571-272-9939. The examiner can generally be reached on M-F 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Jeffrey Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Oluwatosin Ogunbiyi

Examiner

Art Unit 1645

PATRICIA A. DUFFY
PRIMARY EXAMINER